solely to expedite prosecution of the instant application and without prejudice to pursuing these claims in continuing and other related applications. The newly added claims find support in the claims as originally filed and in the sequences provided.

Sequence Compliance

The Examiner has stated that the Sequence Listing previously filed on January 15, 2002 does not include the Sequence shown as Figure 1. Applicants provide herewith a corrected Paper Copy of the Sequence Listing and a Computer Readable Form (CRF) thereof. Applicants' agent states that the contents of the corrected Paper Copy of the Sequence Listing and are identical and that the Sequences Listing and CRF do not go beyond the disclosure as originally filed. Applicants provide above an amendment indicating the sequence listed the appropriate Sequence Identifier.

Rejection of Claims 15-16 and 18-23 Under 35 U.S.C. § 112, Second Paragraph

Claims 15-16 and 18-23 are rejected under 35 U.S.C. § 112, second paragraph. The Examiner states a number of grounds for these rejections.

Claims 15-16 and 18-23: "lacking...residues 1, 1-2, 1-3, or 1-4"

The Examiner asserts that claims 15-16 and 18-23 are indefinite in reciting "lacking...residues 1, 1-2, 1-3, or 1-4." The Examiner asserts that it is unclear whether the claims are limited to only deletions of residues, 1, 1-2, 1-3, or 1-4, respectively, or whether the claims are directed to proteins which may also comprise additional deletions. Applicants respectfully submit that the rejection is now moot in view of the language of the newly added

Claims 15-16 and 18-23: "naturally occurring RANTES"

The Examiner rejects claims over the use of the term "naturally occurring RANTES." Although Applicants traverse the rejection, the term "naturally occurring" has been deleted from the newly added claims as being redundant in view of the recitation of SEQ ID NO. 2. Therefore, Applicants respectfully submit the rejection is now moot and respectfully request that the rejection be reconsidered and withdrawn.

Rejection of Claims 15-16, 18 and 22 Under 35 U.S.C. § 102(a)

Claims 15-16, 18 and 22 are rejected as being anticipated by Oravecz, et al., J. Exp. Med. 186: 1865-1872, 1997 ("Oravecz"). The Examiner asserts that Oravecz teach an amino-terminally truncated RANTES lacking amino acid residues 1-2 of the amino acid sequences of the naturally occurring RANTES of SEQ ID NO:2 and that this truncated RANTES is a potent antagonist of HIV-1. Although the Examiner acknowledges that Applicants have an effective priority date to September 29, 1997 for a truncated form of RANTES lacking residues 1 and 2 (RANTES 3-68), the Examiner states that the priority date of claims 15-16 and 18-23 is considered to be September 28, 1998. Applicants respectfully traverse this grounds of rejection. Oravecz is cited for the proposition of teaching RANTES 3-68 and discloses this truncated form of RANTES after the effective priority date to which the Examiner herself acknowledges Applicants are entitled. Therefore, Oravecz cannot be prior art for truncated forms of RANTES 3-68. To the extent that Oravecz might be cited as prior art against other types of truncated forms of RANTES, Oravecz does not teach these forms and therefore cannot be cited as an anticipating reference under 35 U.S.C. § 102. Accordingly, Applicants respectfully submit that

Claims 15-18 and 21 are also rejected as being anticipated by Noso, et al., J. Immunol. 156: 1946-1953, 1996 ("Noso"). The Examiner asserts that Noso teaches an amino-terminally truncated RANTES consisting of 66 amino acids and derived from dermal fibroblasts. The Examiner asserts that the amino acid sequence of SEQ ID NO: 3 would be an inherent property of the RANTES taught by Noso since Figure 3 of Noso indicates that amino acids 1 and 2 are missing from the protein. The Examiner asserts that an isolated form is taught at page 1950.

Applicants respectfully submit that the rejection of claims 15-18 and 21 is moot as the claims are now cancelled. However, Applicants respectfully traverse the rejection as it might be applied to newly added claim 27 and claims dependent thereon.

Noso does not disclose an isolated polypeptide which has chemokine antagonistic activity. Noso is unable to demonstrate chemokine antagonistic activity in the fraction collected which comprises RANTES amino acids 3-68 along with other impurities which leads Noso to state that "the loss of the two N-terminal residues, serine and proline, does *not* affect Eo-chemotactic activity of RANTES" (emphasis added). Accordingly, because Noso does not teach an isolated form of RANTES (as evidenced by the fact that Noso is unable to obtain antagonistic activity) as recited in the claims, the reference does not teach each element of the claims as required under section 102. Further, because Noso does not obtain antagonistic activity, Noso provides no motivation to further purify the fractions he obtained to provide a truly isolated truncated RANTES polypeptide as recited in the claims. Accordingly, Applicants respectfully submit that the rejection is improper and should be reconsidered and withdrawn.

Claims 15-16, 18-20, and 22 are rejected under 35 U.S.C. § 102(b) as being anticipated by Gong, et al., J. Biol. Chem. 271: 1051-10, 1996 ("Gong"). The Examiner asserts that Gong teach amino terminally truncated RANTES lacking N-terminal amino acids corresponding to amino acid residues 1, 1-2, 1-3, or 1-4, and having chemokine antagonistic activity. The Examiner asserts that this rejection is applicable as the claims are not limited to amino terminally truncated proteins which are deleted only for residues 1, 1-2, 1-3, or 1-4. Applicants traverse the rejection.

Gong teaches amino acids 9-68 of RANTES. As amended the claims require, at least amino acids 5-68 of RANTES. Because Gong does not teach all of the elements of the claims, Applicants respectfully submit a rejection under 35 U.S.C. § 102 is improper and should be reconsidered and withdrawn.

Rejection of Claims 15-16 and 18-23 Under 35 U.S.C. § 102(e)

Claims 15-16 and 18-23 are rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 5,739,103 by Rollins, et al. ("Rollins"). The Examiner asserts that Rollins teach amino-terminally truncated chemokines having antagonistic activity, including RANTES and that truncations may be about 1 to about 10 or about 2 to about 7 amino acids. The Examiner further asserts that by teaching recombinant production of the truncated chemokines in eukaryotic cells, this inherently provides a glycosylated protein. Applicants traverse the rejection.

Applicants respectfully submit that the rejection is moot in view of the cancellation of claims 15-16 and 18-23 and traverse the rejection to the extent that it might be applied to the newly added claims. Rollins does not teach the specific truncations claimed in Applicants'

chemokine truncated anywhere in the range described above *might* inhibit binding and *might or might not* function as an inhibitor (see, column 3, line 20, where Rollins acknowledges that the suggested truncated chemokines may or may not inhibit activation of a chemokine receptor responsive to the corresponding endogenous chemokine). However, the only chemokine taught by Rollins is MCP-1. As stated at section 2121.01 of the MPEP, the inquiry in determining whether or not a reference anticipates an invention is to determine whether the reference contains an enabling disclosure. A mere suggestion that a possible range of amino acid truncations in a broad class of different types of chemokines may or may not possess inhibitory activity does not constitute such a disclosure. Accordingly, Applicants respectfully submit that the rejection is improper and should be reconsidered and withdrawn.

Rejection of Claims 15-23 Under 35 U.S.C. § 103(a)

The Examiner asserts that claims 15-23 are unpatentable over Gong for obviousness. The Examiner acknowledges that Gong does not teach an amino-terminally truncated RANTES having the amino acid sequence of SEQ ID NO.3. However, the Examiner asserts that Gong teach that the functional activity of RANTES is encoded in amino acids 1-5, since various truncations which included amino acids 1-5 resulted in forms of RANTES involving amino acid residues 1-7, 1-8, 1-9, and 1-10 results in binding by these truncated forms of RANTES to receptors they would not ordinarily bind to. The Examiner asserts that this causes Gong to conclude that the "specificity of RANTES lay within residues 1-6." The Examiner further asserts that Gong teach screening of the various truncation sin several assays "which permit determination of whether a truncated form of RANTES is an antagonist and how efficiently that particular truncation functions as an antagonist relative to other RANTES truncations." The

motivated to produce and screen for truncations given the teachings of Gong that multiple amino acid truncations of RANTES have chemokine antagonistic activity. The Examiner states that ordinary artisan would have had a reasonable expectation of success in producing the claimed invention, as a matter of routine optimization.

Applicants respectfully traverse the rejection. Gong's statement on page 10523 that residues 1-5 are essential for the "functional activities" of RANTES does not provide a reasonable expectation that truncations as claimed in the present invention would function as chemokine antagonists. Gong, in fact, shows varying efficiencies of displacement of labeled chemokines by truncated forms of different kinds of chemokines, i.e., varying degrees of inhibition of binding of labeled RANTES and MCP-1 to chemokine receptors (see, Figure 6 of Gong). The truncation with the fewest amino acids removed (i.e., RANTES polypeptides consisting of residues 6-68) showed the *least* displacement and therefore the *least* amount of inhibition. Therefore, contrary to the Examiner's assertion, one of skill in the art would *not* be motivated to make truncations with fewer than six amino acids in *any* chemokine to obtain an effective chemokine inhibitor given Gong's s teachings that the shortest RANTES polypeptide (e.g., 9-68 amino acids) had the highest affinity for chemokine binding sites (see, page 10525, column 1, lines 13-15) and that longer RANTES polypeptides functioned less effectively as inhibitors. Thus, Gong's teachings would not provide the ordinary artisan with a reasonable expectation that using shorter truncations would provide effective inhibitors. Accordingly, Applicants respectfully submit that the rejection is improper and should be reconsidered and withdrawn.

CONCLUSION

Applicants submit that the claims are allowable and that the Application is now in condition for allowance. Applicants respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicants' agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned agent of record.

Date: Jan. 22, 2003 By: _____

Peter F. Corless (Reg. No. 33,860)
EDWARDS & ANGELL, LLP
PO BOX 9169
Boston, Massachusetts 02209
(617) 523-3400

Customer No: 21,874
BOS2_302615.1

Marked-Up Section of Specification Showing Changes Being Made

At page 7, please delete line 6,

[Figure 1: it shows the amino acid sequence of RANTES. Signal sequences are reported]

and insert therefore:

--Figure 1: it shows the amino acid sequence of RANTES (SEQ ID NO. 1). Signal sequences are reported--